

## Remarks

### Claim status

Claims 1-6, 9-12, and 18-21 were pending in this Application. Claims 1-6, 9-12, and 18-21 stand rejected on arguments laid out in the Office Action mailed June 11, 2009. Claims 2-28 were added by the response submitted on October 13, 2009.

### Amendments to the claims

Claim 12 is cancelled without prejudice by the present amendment. Accordingly, after entrance of the present Amendment, claims 1-4, 9, 18, and 22-28 are pending and are presented for examination.

### In-person interview and Rejections for obviousness

Applicants thank Examiners Ronald Niebauer and Anish Gupta for graciously agreeing to an in-person interview with Applicants' representative on October 26, 2009 in the above-referenced case. During the interview, Applicants' representative and the Examiners discussed the outstanding rejection under 35 U.S.C. § 103.

One particular aspect of the rejection that was discussed was the position that "One would have been motivated to combine the chemotherapeutic agent temozolomide as taught by Stupp into the method/compositions of Samoylova since both references deal with *therapeutics specifically of brain tumors*". Applicants had explained that, actually chlorotoxin itself (*i.e.*, unconjugated to a radiolabel and/or cytotoxic moiety) was *not* considered to be therapeutically active against cancer cells.. The Examiners indicated that data and/or tertiary references confirming that, at the time the present application was filed, chlorotoxin alone was not believed to have anti-cancer therapeutic effect would be helpful in overcoming the obviousness rejection.

Responsive to this request, Applicants provide US Patent Number 6,870,029 (filed on October 4, 2001 and published on May 30, 2002). As can be seen with reference to Figure 8 of this patent, when chlorotoxin *alone* was incubated with astrocytoma cells, cell proliferation *increased*. Different channel blockers and the known anti-mitotic agent Ara-C led to decreases

in cell proliferation in the same assay. Clearly, an agent that *increases* cell proliferation would not be expected to have an anti-cancer therapeutic effect.

A second aspect of the §103 rejection discussed during the interview of October 26, 2009, was Applicants' point that the specification clearly shows a *synergistic* effect of chlorotoxin and temozolomide (TEMODAR™) in the treatment of cancer. The Examiners requested that Applicants explain how the data presented in the application illustrate this synergistic effect. Applicants respectfully direct the Examiners' attention to Figure 2 and Example 3. Figure 2 shows that though chlorotoxin treatment alone or TEMODAR™ treatment alone had negligible effects on tumor volume as compared to that observed with saline treatment, a combination of chlorotoxin and TEMODAR™ treatment dramatically decreased tumor growth. Applicants note that Figure 1 also shows that chlorotoxin alone does not have an effect on tumor cell proliferation, though not all controls were shown.

Taken together, one of ordinary skill in the art would understand from reading the specification that the claimed invention is not obvious from what was known in the art at the time of filing.

In conclusion, the present application surprisingly demonstrates synergy in anti-cancer activity between an agent thought to be *pro-proliferative* and an additional anti-cancer agent.

### Conclusion

For all of these reasons, the rejections are not applicable to the claims and the claims should be allowed. A Notice to that effect is earnestly solicited.

Applicants believe that no fees are due with this response. Should any fees be required to maintain pendency and/or to protect the filing date of this application, please consider this a conditional petition therefore and authorization to debit Deposit Account No. 03-1721, referencing Attorney Docket No. 2006636-0026. No authorization is provided to charge *optional* fees (*e.g.*, claims fees); should the PTO be of the view that additional fees are required, a Notice to that effect is respectfully requested.

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